

Association of serum ferritin levels with severity of hypertensive retinopathy

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Abstract:

Introduction: Hypertension is the most important public health problem in developing and developed nations. High blood pressure is defined as BP greater than or equal to 140/90 mm Hg following repeated examination and it applies to all adults (more than 18 years old). Hypertensive retinopathy is one of the micro vascular complications of hypertension, which if left untreated, can lead to retinal vascular occlusion, ischemic optic neuropathy and vitreous haemorrhage. The present study assesses the association of serum ferritin levels with severity of hypertensive retinopathy. **Objective:** To study the correlation between serum ferritin levels and hypertensive retinopathy. **Material and methods:** The present study was conducted prospectively in the Upgraded Department of Ophthalmology, Government Medical College, Jammu for a period of 1 year w.e.f 1st November 2021 to 31st October 2022. All patients, aged above 18 years diagnosed with hypertension (JNC 8 Criterion) attending the OPD of upgraded Department of Ophthalmology, Government Medical College, Jammu for fundoscopic examination with complaints of diminution of vision were included in the study. The cases were non selective with regards to sex, ethnic origin, and occupation and controls included normotensives above 18 years age without any other systemic illness. **Exclusion criteria:** The study excluded patients with age < 18 years, those in whom dilatation of pupil is contraindicated, Primary open angle glaucoma and angle closure glaucoma, patients with hazy media with impaired visualization of fundus, patients having diabetes mellitus, liver or kidney disease, dyslipidaemia, recent surgery, cerebral disease, anaemia, stroke, pregnant and lactating females and patients taking iron in oral or i/v formulation. **Results:** The present study was conducted in 50 patients with hypertensive retinopathy and 50 controls without HR. The mean age of the patients with HR was 56.42±10.90 years and we observed a male predominance. No significant difference was seen among both the groups with respect to age (p=0.93) and gender (p=0.216). The BMI in cases was 28.02±2.91 while in control it was 26.58±2.06. The BMI index was significantly more in cases than control. The SBP in cases was 157.96±11.13 while in controls, it was 117.36±7.34. When the SBP was compared between the grade 1 hypertensive retinopathy (157.36±10.35) and grade 2 HR (158.56±12.03), no significant difference was observed. Similar trends were observed with DBP. The mean DBP of control was 112.20±8.16 (grade 1 HR : 112±9.01 vs grade 2 HR: 112.40±7.39) while in controls, the mean DBP was 79.86±4.00. The difference of SBP and DBP was highly significant (p<0.001). In present study we observed that FBS, Total cholesterol, HDL, triglyceride, CRP doesn't show any significant difference among cases and control. Whereas creatinine and LDL were significantly more in cases (although in normal range in both the groups). Serum ferritin was significantly more in cases (87.68±51.64 ng/dl) than in controls (63.98±20.92 ng/dl). However, it was observed that when grade 1 (80.20±36.45) and grade 2 HR (95.16±63.24) were compared, subjects with grade 2 hypertensives showed more serum ferritin levels than grade 1, although the comparison was not statistically significant. **Conclusion:** Our study suggests that there is a relationship between HR and

ferritin level, which may be associated with an increased level of oxidative stress. Hence the estimation of the serum ferritin levels can help the medical professionals to predict early development of hypertension as well as hypertensive retinopathy.

Introduction:

Hypertension is the most important public health problem in developing and developed nations. High blood pressure is defined as BP greater than or equal to 140/90 mm Hg following repeated examination and it applies to all adults (more than 18 years old). Over 90% of patients with high blood pressure have primary hypertension which is idiopathic. Primary hypertension cannot be cured, but it can be controlled with appropriate therapy (including lifestyle modifications and medications). Hypertensive retinopathy is one of the microvascular complications of hypertension, which if left untreated, can lead to retinal vascular occlusion, ischemic optic neuropathy and vitreous hemorrhage (Bell K *et al.*, 2015). The first attempt to relate the retinal vascular changes to survival in the hypertensive population was done by Keith, Wagner and Barker in 1939. They divided hypertensive patients into four groups on the basis of the ophthalmoscopic characteristics of each group. This grouping is correlated directly with the degree of systemic hypertension and inversely with the prognosis for survival (Sihota R *et al.* 2020).

Grade 1: Mild to moderate narrowing or sclerosis of the smaller arterioles.

Grade 2: Moderate to marked narrowing of the retinal arterioles; exaggeration of the light reflex; changes at the arteriovenous crossings.

Grade 3: Retinal arteriolar narrowing and focal constriction, prominent arteriovenous crossing changes, retinal oedema, cotton-wool spots, flame-shaped hemorrhages.

Grade 4: All the features of Grade 3 are seen, as well as papilledema. This classification is still in use today and is widely accepted.

Numerous physiological processes are involved in the pathogenesis of hypertensive retinopathy. One of them is a high level of oxidative stress, which is shown by an increase in plasma markers like ferritin and gamma-glutamyl transferase [Karaca *et al.*, 2013; Coban *et al.*, 2010]. Other significant mechanisms include low-grade inflammation and increased platelet activation (Coban E *et al.*, 2010).

Objective:

To study the correlation between serum ferritin levels and hypertensive retinopathy.

Material and methods:

The present study was conducted prospectively in the Upgraded Department of Ophthalmology, Government Medical College, Jammu for a period of 1 year w.e.f 1st November 2021 to 31st October 2022. All patients, aged above 18 years diagnosed with hypertension (JNC 8 Criterion) attending the OPD of upgraded Department of Ophthalmology, Government Medical College, Jammu for fundoscopic examination with complaints of diminution of vision were included in the study. The cases were non selective with regards to sex, ethnic origin, and occupation and controls included normotensives above 18 years age without any other systemic illness. Ocular examination (Visual acuity, slit lamp examination, Fundus examination) and biochemical tests (Serum ferritin, CBC, KFT, LFT, FBSetc.) were carried out in all patients.

Exclusion criteria:

The study excluded patients with age < 18 years, those in whom dilatation of pupil is contraindicated, Primary open angle glaucoma and angle closure glaucoma, patients with hazy media with impaired visualization of fundus, patients having diabetes mellitus, liver or kidney disease, dyslipidaemia, recent surgery, cerebral disease, anaemia, stroke, pregnant and lactating females and patients taking iron in oral or i/v formulation.

Results:

The present study was conducted in 50 patients with hypertensive retinopathy and 50 controls without HR. The mean age of the patients with HR was 56.42±10.90 years and we observed a male predominance. No significant difference was seen among both the groups with respect to age (p=0.93) and gender (p=0.216). The BMI in cases was 28.02±2.91 while in control it was 26.58±2.06. The BMI index was significantly more in cases than control. The SBP in cases was 157.96± 11.13 while in controls, it was 117.36±7.34. When the SBP was compared between the grade 1 hypertensive retinopathy (157.36±10.35) and grade 2 HR (158.56±12.03), no significant difference was

observed. Similar trends were observed with DBP. The mean DBP of control was 112.20 ± 8.16 (grade 1 HR : 112 ± 9.01 vs grade 2 HR: 112.40 ± 7.39) while in controls, the mean DBP was 79.86 ± 4.00 . the difference of SBP and DBP was highly significant ($p < 0.001$). In present study we observed that FBS, Total cholesterol, HDL, triglyceride, CRP doesn't show any significant difference among cases and control. Whereas creatinine and LDL were significantly more in cases (although in normal range in both the groups).

Serum ferritin was significantly more in cases (87.68 ± 51.64 ng/dl) than in controls (63.98 ± 20.92 ng/dl). However, it was observed that when grade 1 (80.20 ± 36.45) and grade 2 HR (95.16 ± 63.24) were compared, subjects with grade 2 hypertensives showed more serum ferritin levels than grade 1, although the comparison was not statistically significant.

Table 1 shows the age distribution of the study population.

Age group	No. of patients	Percentage of patients
≤ 40	9	9
41-50	26	26
51-60	29	29
61-70	25	25
71-80	8	8
>80	3	3
Total	100	100

Table 2: Distribution of study population according to gender

Sex	No. of patients	Percentage of patients
Female	38	38.0
Male	62	62.0
Total	100	100.0

Table 3: Distribution of study population according to hypertensive retinopathy

Study population	Group	No. of patients	Percentage of patients
Cases	Grade 1 hypertensive retinopathy	25	25
	Grade 2 hypertensive retinopathy	25	25
Control	No hypertensive retinopathy	50	50
	Total	100	100

Table 4: Comparison of BMI among both the groups

BMI	CASES		CONTROL		TOTAL		Chi Square	P- Value
	n	%	n	%	n	%		
Normal weight (18.5-24.9)	7	14.0%	10	20.0%	17	17.0%	8.61	0.013
Overweight (25-29.)	29	58.0%	37	74.0%	66	66.0%		
Obese (>29.9)	14	28.0%	3	6.0%	17	17.0%		
Total	50	100.0%	50	100.0%	100	100.0%		

Table 5: Comparing grouped data variable among both the groups

	Cases (n=50)		Control(n=50)		t-value	p-value
	Mean	Sd	Mean	Sd		
BMI	28.02	2.91	26.58	2.06	2.86	0.01
SBP	157.96	11.13	117.36	7.34	21.54	<0.001
DBP	112.20	8.16	79.86	4.00	25.15	<0.001
FBS	88.60	6.97	87.38	9.23	0.75	0.46
S.CREATININE	0.80	0.14	0.65	0.23	3.77	<0.001
Total cholesterol (mg/dl)	166.08	15.24	164.74	12.28	-4.04	0.62
LDL (mg/dl)	95.84	12.43	91.52	5.57	-2.24	0.03
HDL (mg/dl)	46.62	8.46	44.40	7.21	1.41	0.16
Triglyceride (mg/dl)	133.26	25.02	129.54	24.02	0.76	0.45
C-reactive protein (mg/dl)	0.42	0.25	0.38	0.14	1.08	0.28
Ferritin (ng/ml)	87.68	51.64	63.98	20.92	3.01	<0.001

Table6: Comparing grouped data variable among grade 1 and grade 2 hypertensive retinopathy

	Grade 1 hypertensive(n=25)		Grade 2 hypertensive(n=25)		t-value	p-value
	Mean	Sd	Mean	Sd		
AGE	56.60	11.02	56.24	11.05	0.12	0.91
BMI	27.88	2.85	28.16	3.02	-0.34	0.74
SBP	157.36	10.36	158.56	12.03	-0.38	0.71

DBP	112.00	9.02	112.40	7.39	-0.17	0.86
FBS	88.68	6.64	88.52	7.42	0.08	0.94
S.CREATININE	0.80	0.12	0.79	0.16	0.30	0.77
Total cholesterol (mg/dl)	165.04	11.58	164.44	13.18	0.17	0.86
LDL (mg/dl)	91.28	5.76	91.76	5.49	-0.30	0.76
HDL (mg/dl)	46.72	8.81	46.52	8.27	0.08	0.93
Triglyceride (mg/dl)	135.68	27.90	130.84	22.07	0.68	0.50
C-reactive protein (mg/dl)	0.39	0.17	0.44	0.31	-0.69	0.49
Ferritin (ng/ml)	80.20	36.45	95.16	63.24	-1.02	0.31

Discussion:

The present case control study was conducted in Department of Ophthalmology, Government Medical College, Jammu among patients who underwent fundoscopic examination with complaints of diminution of vision. The aim of the study was to evaluate serum ferritin levels in patients with hypertensive retinopathy and normotensive patients. We also assessed the correlation between serum ferritin levels and hypertensive retinopathy.

Total 100 subjects were included in the study i.e 50 cases and 50 controls. 25(25%) had grade 1 hypertensive retinopathy while 25(25%) had grade 2 hypertensive retinopathy. 50(50%) patients without hypertensive retinopathy were taken as controls.

The mean age of the patients with hypertensive retinopathy was 56.42 ± 10.90 years with a male predominance. The age and sex matched controls were included in the study. The previous studies also showed that hypertensive retinopathy is more common in sixth decade of life.

A study by **Jeganathan et al., (2010)** also showed that the prevalence of retinopathy peaked between the ages of 50 and 69 years with a male predominance.

Similarly, **Pun CB et al., (2019)** also reported the mean age of the patients to be 60.58 ± 12.26 years in hypertensive retinopathy.

It was observed that more cases (28%) had BMI >29.9 i.e. obese category than controls (6%) while overweight subjects were more in control group (74%) than cases. 20% of controls have normal weight while only 14% of cases had a normal weight. The difference between both the groups was statistically significant. ($p=0.013$). The BMI in cases group was 28.02 ± 2.91 [(grade 1 HR): 27.88 ± 2.84 ; vs (grade 2 HR): 28.18 ± 3.02] while in control it was 26.58 ± 2.06 . The BMI was significantly more in cases than control.

Tibbling et al., (1967) in their study reported that weight was correlated significantly with the prevalence of hypertensive retinopathy, which was in association with present study.

The SBP in cases was 157.96 ± 11.13 mmHg while in control group it was 117.36 ± 7.34 mmHg. The mean DBP of cases was 112.20 ± 8.16 while in controls, it was 79.86 ± 4.00 . The difference of SBP and DBP was highly significant ($p < 0.001$) between cases and controls. When the SBP was compared between the grade 1 hypertensive retinopathy (157.36 ± 10.35) and grade 2 HR (158.56 ± 12.03) no significant difference was observed.

The results of the present study were in accordance with **Coban et al., (2010)** who showed the SBP of grade 1 HR to be 148 ± 4 mmHg while grade 2 to be

149±4mmHg and controls to be 127±6mm of hg. Their findings were similar to our study and cases (grade1 +grade 2) had significantly more SBP than controls.

Similar findings were shown by **Jhang *et al.*, (2018)** who showed mean SBP of cases to be 156.00 ± 19.01 while in controls it was 149.19 ± 14.34mmHg.

In present study we observed that FBS, Total cholesterol, HDL, triglyceride, CRP don't show any significant difference among cases and controls. These results were in accordance with the study conducted by **Coban *et al.*, (2010)**.

In present study we observed that Serum ferritin levels was significantly more in cases (87.68±51.64 ng/dl) than in controls (63.98±20.92ng/dl). However, it was observed when grade 1(80.20±36.45) and grade 2 HR(95.16±63.24) were compared, subjects with grade 2 hypertensives showed more serum ferritin levels than grade 1, although the comparison was not statistically significant.

Coban *et al.*,(2010) observed serum ferritin levels in grade 1 HR patients to be 77.8±23.7ng/ml while for grade 2 HR it was 92.9±31.8 ng/dl. For controls the value of serum ferritin was 59.9±19.2ng/ml. The serum ferritin levels were significantly more in grade 1 and grade 2 when compared to control group which was in accordance to the present study.

Conclusion:

Our study suggests that there is a relationship between HR and ferritin level, which may be associated with an increased level of oxidative stress. Oxidative stress, a mechanism known to be involved in vascular lesions, may promote the development of HR.

Present study showed that the elevated serum ferritin levels were positively correlated to the SBP and DBP (p value= <0.05) because the elevated

ferritin levels increase with increase in BP. Increased ferritin levels causes vascular oxidative stress and impair vaso-reactivity, which leads to inflammation, endothelial damage and consequently atherosclerosis leading to BP elevation. Hence the risk of incident hypertension was proportional to the serum ferritin level as an early predictor of the development of hypertension. Hence the estimation of the serum ferritin levels can help the medical professionals to predict early development of hypertension as well as hypertensive retinopathy.

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